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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/712,447	11/13/2003	Gattadahalli M. Anantharamiah	21085.0143U2	8707

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EXAMINER	
KOLKER, DANIEL E	
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11/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/712,447	ANANTHARAMIAH ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5,6 and 14-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6 and 14-17* is/are rejected.

7)☒ Claim(s) *5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The remarks, amendments, and declaration filed 4 September 2007 have been entered. Claims 4, 7 – 13, and 18 – 34 are canceled; claims 1 – 3, 5 – 6, and 14 – 17 are pending and under examination.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4 September 2007 has been entered.

New Rejections

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "capable of forming an amphipathic α helical structure". It is unclear what the term "capable of" means. One the one hand, the claim could be interpreted as only including those sequences which in fact form such helices; on the other hand, the claim might also include proteins which do not themselves for amphipathic α helices, but after further modification or binding with some other molecule are incorporated into the helices. The latter could be "capable of" forming the helices, even though they do not on their own form such helices. If applicant is attempting to claim peptides which form such helices, it is recommended that claim 1 be amended to recite "wherein the polypeptide forms an amphipathic α helical structure." However as written it is not clear what the scope of desired patent protection for claim 1 is.

Claim 3 is confusing because it recites "wherein the polypeptide comprises from 14 to 18 amino acids in length." It is unclear whether 14 to 18 amino acids is to be the maximum length

of the polypeptide, or whether this is a minimum length. On the one hand, the term "14 to 18 amino acids in length" seems to limit the length of the protein. But at the same time, when coupled with "comprising" language, which allows for any number of additional residues to be added to either side of the protein of SEQ ID NO:210, the "14 to 18" limitation appears to set a minimum number of residues. The length of the polypeptides encompassed by claim 3 is unclear.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 – 3, 6, and 14 – 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to peptides which mimic apolipoprotein E and which have certain structural features, as recited in claim 1. Claim 1 requires that the peptides be "capable of" forming a certain helix. The specification discloses several proteins within the scope of claim 1 (including SEQ ID NO:2, 5, 8, and 10 among others), but does not describe the full breadth of the genus of polypeptides claimed. The specification fails to disclose what additional residues are to be added at either the N- or C-terminus of the claimed peptide. The use of "comprising" language allows for additional residues, but the specification fails to describe which residues should be added or should be avoided. The proteins encompassed by independent claim 1 are complex three-dimensional structures. Whether the protein will fold into an amphipathic alpha helix depends not only upon which structures are present in the 14 amino acids of SEQ ID NO:210, but also on which additional residues are present. As the protein chain is built, the charges present on other amino acid residues outside of the 14 residues in SEQ ID NO:210 will influence the shape of this region. The specification does not disclose to the public which residues are required, or which should be avoided, in the additional sequence elements to be added, such that an amphipathic alpha helix is maintained.

Additionally, claim 1 is necessarily broader than claims 14 and 15. The specification fails to disclose to the public which structural elements in the scope of claim 1 but are not in claims 14 – 15. While certain examples of LDL-decreasing polypeptides are given in the specification, there is no description of the features which are in the broader genus of claim 1 but are not in the narrower sub-genus of claims 14 – 15.

A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

As the specification does not disclose the structure of those proteins which comprise SEQ ID NO:210 but do not either enhance binding or degradation of LDL or VLDL, the specification does not provide evidence of possession of the broad genus of proteins encompassed by claim 1.

Maintained Rejections

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 – 3, 6, and 16 – 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the protein of SEQ ID NO:5, and for proteins comprising SEQ ID NO:210 which also enhance binding or degradation of LDL or VLDL, does not reasonably provide enablement for the full scope of proteins comprising SEQ ID NO:210 as recited in claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection stands for the reasons of record. Briefly, independent claim 1 is quite broad. The protein of SEQ ID NO:210 only requires that four amino acid residues be explicitly defined, the other ten can be any hydrophobic residue. The claim does not require that the invention have any particular function, only that it be "capable of" forming a certain shape. The claim reads on a large number of embodiments which the specification does not teach how to use. While the specification asserts that the claimed invention is useful for decreasing cholesterol, only dependent claims 14 – 15 are reasonably on point to LDL and VLDL, two types of cholesterol. Claim 1 is necessarily broader than claims 14 – 15, and therefore encompasses all those peptides which comprise SEQ ID NO:210, are "capable of" forming α helices, and do not modulate LDL or VLDL binding or degradation.

The art of record indicates that α helices are very abundant and involved in a plethora of physiological functions. See for example Bechinger (2000, of record), as well as Kandel (1991, of record). The biochemical roles of α-helix-containing proteins include antibiotics, transcription factors, and channels. The roles are so diverse that the skilled artisan would need to determine, on his or her own, how to use each of the proteins encompassed by SEQ ID NO:210. The specification does not provide adequate guidance or working examples commensurate with the full scope of claim 1, therefore the artisan would have to resort to undue experimentation to determine how to use these proteins.

Applicant traverses this rejection on pp. 7 – 10 of the remarks filed 4 September 2007. Applicant specifically makes the following arguments:

1. The office has failed to meet its burden in rejection the claims under 35 USC 112, first paragraph, because the examiner has not presented any evidence that the claimed polypeptides would be unable to enhance binding of LDL or VLDL.

2. All embodiments within the scope of the claim need not be operable.

3. The declaration filed under 37 CFR 1.132 indicates that the structures which contain Arg on their polar face allow the claimed polypeptides to associate with LDL and VLDL.

Applicant's arguments have been fully considered but they are not persuasive. With respect to point number 1 above, applicant is arguing limitations which are not in claim 1. The examiner cited several references which indicate that α-helix-containing proteins have a wide range of biochemical roles within the cell and the body. Claim 1, which is necessarily broader than claims 14 – 15, includes any and all proteins with the sequence of SEQ ID NO:210 and which form an amphipathic α-helix. There is no requirement that the protein be able to bind LDL or VLDL. The claim includes a large number of embodiments which the specification does not disclose how to use. The skilled artisan would have to discover, on his or her own, how to use those proteins which are within the scope of claim 1 but not in the scope of claims 5 and 14 – 15.

With respect to point number 2, it is of course true that a claim can contain non-enabled embodiments and still be considered to be enabled. However, as the number of embodiments which are not enabled grows, it is proper to consider whether or not the specification teaches the public how to use the full scope of the claim. Applicant is directed to MPEP § 2164.08(b), which states in part "However, claims reading on significant numbers of inoperative embodiments would render claims nonenabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative." As claims 1 – 3, 6, and 16 – 17 include proteins which do not bind to or decrease LDL or VLDL, the specification does not teach the public how to use the full scope of the claimed invention. Therefore the examiner properly concluded that the full scope of these claims is not enabled in the absence of undue experimentation.

With respect to point number 3 above, the declaration filed by Dr. Anantharamaiah has been fully considered but it is not persuasive. The declaration under 37 CFR 1.132 filed 4 September 2007 is insufficient to overcome the rejection of claims 1 – 3, 6, and 16 – 17 based upon lack of enablement as set forth in the last Office action because: the declaration is not

commensurate with the full scope of the claims. The declaration discusses two operative peptides, named R-18L and R18L2Y (see paragraphs 3a and 3b) and two inoperative peptides (see paragraphs 4a and 4b). The operative peptides are within the scope of claim 1; however the claim reads on a huge number of possible variants. What is disclosed in the specification and the declaration is narrow, whereas what is claimed is broad. Two working embodiments are shown, but assuming that any X residue can be one of four (glycine, threonine, serine, or alanine) and Y can be any one of six (phenylalanine, tyrosine, leucine, isoleucine, valine, or tryptophan) amino acids, each of which can be independently selected, claim 1 reads on at least 17915904 possible protein sequences (three positions where any one of four residues can be present and seven positions with six possible residues, or $4^3 \times 6^7$). Thus the disclosure of two embodiments, which have similar sequences, is not commensurate with the breadth of the claim.

For the reasons above and previously made of record, the full scope of claims 1 – 3, 6, and 16 – 17 is not enabled in the absence of undue experimentation.

Conclusion

6. Claims 1 – 3, 6, and 14 – 17 are rejected.

7. Claims 5 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Daniel E. Kolker, Ph.D.
November 13, 2007

ROBERT C. HAYES, PH.D.
PRIMARY EXAMINER